

### REMARKS

Claims 1-3, 5-16, 33-44 and 47-50 are pending in the above-identified patent application. Claim 44 is amended herein. Claims 45 and 46 are canceled by this Amendment. No new matter is introduced, and Applicants' amended claim is fully supported by Applicants' specification.

1. Allowed Claims

The Applicants note with appreciation that claims 1-3, 5-16, 33-43 and 47-50 are allowed.

2. Rejection of Claims Under 35 USC §112, First Paragraph

The Examiner rejected claim 44-46 under 35 USC §112, first paragraph as not being enabled by Applicants' specification for treatment of all of the recited CNS diseases in claims 44 and 45, or for the gastrointestinal diseases of claim 46. Applicants have canceled claims 45 and 46, and have amended claim 44 to recite, more specifically, a method for treating memory disorders, including Alzheimer's disease, by administration of an effective amount of a compound of claim 1 to a subject in need thereof.

The link between the 5-HT<sub>6</sub> receptor and cognitive/memory disorders, including Alzheimer's disease, is well established and the effectiveness of 5-HT<sub>6</sub> receptor antagonists in memory enhancement and memory repair has been demonstrated. At least three selective 5-HT<sub>6</sub> receptor antagonists are currently undergoing clinical trials for treatment of memory dysfunction and Alzheimer's disease: GSK 742457 (Glaxo Smith Klein, Phase I); M100907B (Aventis Pharmaceutical, Phase I); and SGS518 (Saegis Pharmaceutical, Phase I). The Glaxo Smith Kline selective 5-HT<sub>6</sub> antagonist SB-271046 has recently been dropped from clinical trials.

The link between treatment of memory disorders and the 5-HT<sub>6</sub> receptor is well established in the Scientific literature. Enhanced retention of spatial learning in rats following administration of a 5-HT<sub>6</sub> antagonist has been specifically shown by Woolley et al., "A Role for 5-HT<sub>6</sub> Receptors in Retention of Spatial Learning in the Morris Water

Maze", Neuropharmacology 41, 210-219 (2001). The memory enhancing effects of 5-HT6 antagonists in the water maze test were also confirmed by Rogers et al., "5-HT6 Receptor Antagonists Enhance Retention of a Water Maze Task in the Rat", Psychopharmacology 158, 114-119 (2001). Improved learning consolidation in rats subject to autoshaping tasks following treatment with a 5-HT6 receptor antagonist has been shown by Meneses, "Role of 5-HT6 Receptors in Memory Formation", Drug News Perspect. 14(7), 396-400 (2001). Additional exemplary publications linking 5-HT6 antagonists to treatment of memory disorders are: Riemer et al., "Influence of the 5-HT6 Receptor on Acetylcholine Release in the Cortex ", J. Med. Chem. 46, 1273-1276 (2003); Dawson et al., "In Vivo Effects of the 5-HT6 antagonist SB-271046 on Striatal and Frontal Cortex Extracellular Concentrations of Noradrenaline, Dopamine, 5-HT, Glutamate and Aspartate", British J. Pharmacology 130, 23-26 (2000); Branchek et al., "5-HT6 Receptors as Emerging Targets for Drug Discovery", Ann. Rev. Pharmacol. Toxicol. 40, 319-334 (see p. 329 in particular) (2000); Woolley et al., "Reversal of a Cholinergic-Induced Deficit in a Rodent Model of Recognition Memory by the Selective 5-HT6 receptor Antagonist Ro 046790", Psychopharmacology 170, 358-367 (2003); Dawson et al., "5-HT6 Receptor Antagonist SB-271046 Selectively Enhances Excitatory Neurotransmission in the Rat Frontal Cortex and Hippocampus", Neuropsychopharmacology 25 No. 5, 662-668 (2001); and Tsai et al., "Association Analysis of the 5-HT6 receptor polymorphism C267T in Alzheimer's Disease", Neuroscience Lett. 276, 138-139 (1999). Copies of these publications (which predate Applicants' filing date) are submitted herewith.

Accordingly, Applicants respectfully submit that the use of 5-HT6 receptor antagonists for the treatment of memory disorders (including Alzheimer's disease) has been established in the art, and skilled persons can reasonably test such compounds for treatment of memory disorder indications without undue experimentation. Applicants believe that claim 44 as amended meets the criteria of 35 USC §112.

**CONCLUSION**

The Applicants respectfully believe that all claims pending in the above-identified case are now in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

No fees should be due. However, in the event it is determined that a fee is due, please charge same to Deposit Account No. 18-1700.

Respectfully submitted,



Robert C. Hall  
Reg. No. 39,209  
Attorney for Applicants

Roche Palo Alto  
Patent Department, MS A2/250  
Palo Alto, CA 94301  
Phone: (650) 354-7540

Date: September 30, 2005